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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
GAMBEL, PHILLIP	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/874,141	DARRELL ET AL.	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/30/04; 10/19/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,3,5,16-31 and 33-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,3,5,16-31 and 33-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.

Applicant's submission filed on 9/30/04 has been entered.

Applicant's amendment, filed 9/30/04, has been entered.
Claim 32 has been canceled. Claims 1, 4, and 6-15 have been canceled previously.
Claims 2, 3, 24, 30, 31, 33 and 34 have been amended.

Claims 2, 3, 5, 16-31 and 33-39 are pending.

Applicant's election with traverse of multiple sclerosis (Group II-C) as the disease species has been acknowledged.

Claims 2, 3, 5, 16-31 and 33-39 as they read on treating multiple sclerosis with anti-gp39 antibodies are under consideration as the elected invention.

2. As pointed out previously, the filing date of the instant claims is deemed to be the filing date of the provisional application 60/209,584, filed 6/6/00.

Applicant's submission of an updated Application Data Sheet filed 10/19/04, correcting the priority claim and the spelling of the co-inventor Darrell Anderson.

Again, applicant should amend the first line of the specification to delete the reference to the asserted priority document USSN 08/554,850.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Applicant's amended claims, filed 9/30/04, have obviated the previous rejection under 35 U.S.C. § 112, first paragraph, written description / new matter with respect to the recitation of "at least one cytokine by T cells".

5. Claims 2, 3, 5, 16-31 and 33-39 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.

The specification as originally filed does not provide support for the invention as now claimed: "substantially non-agonistic of a T cells activation response(s)"

Applicant's amendment, filed 9/30/04, directs support to Examples 18-21 on pages 55-57 as well as Figures 16-20 of the instant specification. Applicant asserts that one skill in the art would reasonably have regarded the description of the invention in the application as conveying the inventors were in possession of the claimed improved methods comprising screening and identifying anti-gp39 antibodies that are "substantially non-agonistic of the disclosed T cell activation responses".

The phrase "substantially non-agonistic of the disclosed T cell activation responses" is not disclosed in the specification as-filed. In turn, the specification as-filed does not define the phrase nor set forth the metes and bounds of the "limitation".

In addition, "substantially" refers "to a great extent or degree".

However as indicated herein, the phrase "substantially non-agonistic of a T cells activation response(s)" is subject to a rejection under 35 U.S.C. § 112, second paragraph, as well, given that the metes and bounds of said "substantially non-agonistic of the disclosed T cell activation responses" because the parameters are not clearly defined. The "phrase" is a relative in nature in in which the phrase is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

While the citations in the specification relied upon by applicant describe certain experimental observations under certain defined conditions with certain anti-gp39 antibodies (anti-CD40L antibodies), the specification as-filed does not provide a sufficient written description nor set forth the metes and bounds of this "phrase". The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "limitation", as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action

Alternatively, applicant is invited to provide sufficient written support for the "limitation" indicated above. See MPEP 714.02 and 2163.06

Applicant's arguments are not found persuasive.

6. Claims 24-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

It is apparent that the 24-31 antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line / hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty as provided by applicant's amendment filed 9/30/04, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

It does not appear that applicant has provided the appropriate assurances required under 35 USC 112, first parargraph, for the deposit of biological materials. See 37 CFR 1.808 and MPEP 2410.

7. Claims 2, 3, 5, 16-31 and 33-39 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 2, 3, 5, 16-31 and 33-39 are indefinite in the recitation of "substantially non-agonistic of the disclosed T cell activation responses" because the conditions are not clearly defined. The phrase "substantially non-agonistic of the disclosed T cell activation responses" is not disclosed in the specification as-filed. In turn, the specification as-filed does not define the phrase nor set forth the metes and bounds of the "limitation".

In addition, "substantially" refers "to a great extent or degree". The "phrase" is a relative in nature whereby the "phrase" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

In addition, "substantially" refers "to a great extent or degree".

While the citations in the specification relied upon by applicant describe certain experimental observations under certain defined conditions with certain anti-gp39 antibodies (anti-CD40L antibodies) (e.g. see to Examples 18-21 on pages 55-57 as well as Figures 16-20 of the instant specification, the specification as-filed does not provide a sufficient written description nor set forth the metes and bounds of this "phrase", as indicated above.

B) Claim 18 contains the trademark or trade name "PRIMATIZED". Where a trademark or trade name is used in a claims as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 USC 112, second paragraph, See Ex parte Simpson, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark or the trade name "PRIMATIZED" is used to identify or describe a recombinant form of an antibody, and accordingly, the identification or the description is indefinite. The relationship between a trademark or tradename and the product it identifies may be uncertain and arbitrary. The formula or characteristics of the product may change from time to time and yet it may continue to be sold under the same trademark or tradename.

C) Applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter.

Applicant should specifically point out the support for any amendments made to the disclosure. See MPEP 714.02 and 2163.06

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office Action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

9. Upon reconsideration of applicant's amended claims, filed 9/30/04, the previous rejections under 35 U.S.C. § 102(a)(e) as being anticipated by Black et al. (U.S. Patent No. 6,001,358) and under 35 U.S.C. § 102(e) as being anticipated by Noelle et al. (U.S. Patent No. 6,328,964) have been obviated by the addition of reciting the assaying steps.

10. Claims 2, 3, 5, 16-31 and 33-39 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Black et al. (U.S. Patent No. 6,001,358) in view of the art known methods to screen for inhibitors of cytokines and proliferation in view of Schrader et al. (U.S. Patent No. 5,627,052), Burkly et al. (US2002/0028202 A1) and newly added Wilson et al. (U.S. Patent No. 6,372,208 B1).

Black et al. teach methods of treating disease condition wherein gp39 inhibition is therapeutically beneficial (columns 13-14 and 31-34), including multiple sclerosis with column 14, line 40 and column 32, line 67) with antibodies that bind gp39 (CD40 ligand), which block signals delivered via CD40 (See Examples 2, 3 columns 22-23; Examples 11-17 on columns 28-38 (see entire document).

In addition, Black et al. teach chimeric, humanized, and primatized antibodies, including the use of different heavy chain constant regions (IgG1, IgG3, IgG4), with conservative amino acid substitutions such as Kabat positions 229 and 236 as well as the 24-31 antibody specificity and its variable regions amino acid sequences encompassed by the claimed methods (see entire document, including Background of the Invention, including columns 6-7; Summary of the Invention; Detailed Description of the Invention, including columns 13-22; Claims). Further, it is noted that Black et al. teach that it was known that $gp39^+$ T cells produced IL-2, IL-4 and γ-interferon (see column 4, paragraph 1). In addition, Black et al. teach modes of administration and dosages of antagonistic anti-gp39 antibodies encompassed by the claimed methods (see columns 33-38).

Black et al. differs from the claimed methods by not disclosing the art known use of screening for inhibitors of cytokine activity such as IL-2, IL-4 and γ-interferon as well as cell proliferation per se in selecting antagonistic anti-gp39 antibodies.

Schrader et al. teach methods of producing antibodies of a desired function to a variety of antigens, including IL-2 and γ-interferon, including the section of antibodies that neutralizes a growth factor or detection of antibodies that neutralize IL-2 (e.g. see columns 8-9, overlapping paragraph) and exemplifies the detection of antibodies that neutralize IL-2 (see Example 1 on columns 21-22) (see entire document, including Summary of the Invention and Detailed Description of the Invention).

Burkly et al. teach known methods of assaying or screening the ability of antagonists such as antibodies to block a response to a particular cytokine (e.g. IL-2) (See GC Chain Blocking Agents and Production of GC Blocking Antibodies on pages 7-8 and Testing Compounds of the Invention for Biological Utility on page 13). Burkly et al. note that it will be recognized by one skilled in the art, that these screens can be arranged to discover antibodies whose activities are conspicuous in one or more of these assays (see paragraph 095 on page 8) and that one of skill in art may easily determined using well known methods whether a particular blocking agent displays biological activity (see Testing Compounds of the Invention for Biological Utility on page 13).

Newly added Wilson et al. teach that CD40 ligand – CD40 interactions are desirable given its broad activity in both T helper cell activation and function as well as the absence of redundancy in its signaling pathway (see entire document, particularly column 6, paragraphs 4-5). In addition, Example 8 describes analyzing the effect of CD40 ligand blockade with antibodies on T cell activation using both in vitro and in vivo assays, including T cell proliferation (see columns 20-22).

Therefore, it would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Schrader et al., Burkly et al. and Wilson et al. to those of Black et al. to screen and obtain antagonistic anti-gp39 antibodies with the ability to inhibit cytokines produced by activated T cells, including the inhibition of IL-2, IL-4 and γ-interferon, which were known to be products of the T cells targeted by antagonistic anti-gp39 antibodies. According to Black et al., a person of ordinary skill in the art would have been motivated to produce this resultant ability of anti-gp39 antibodies to inhibit cytokine activity by activated T cells in order to test and select for those anti-gp39 antibodies that had the described properties of inhibiting gp39:CD40 interaction and the resultant ability of such antibodies to inhibit T cell mediated activation of immune response in the treatment of various conditions and disorders, including multiple sclerosis. From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's argument's filed 9/30/04 have been fully considered but are not found convincing essentially for the reasons of record and that set forth herein.

Applicant appears to simply argue that the secondary references do not describe or suggest a methods of obtaining anti-gp39 antibodies that comprise performing multiple assays to identify non-agonistic anti-gp39 antibodies encompassed by the claimed methods.

Once a prima facie case of obviousness has been made the burden of going further is shifted to applicant. In re Keller, 208 USPQ 871, 882 (CCPA 1981). This applicant has not done, but rather argues the references individually and not their combination. One cannot show non-obviousness by attacking references individually where the rejections are based on a combination of references. In re Young, 150 USPQ 725 (CCPA 1968). See MPEP 2145.

Obviousness can be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992).

In this case the teachings of the secondary references provide clear teachings of the known assays to test inhibitory antibodies, including antibodies that inhibit T cell activation and proliferation, including antibodies that inhibit CD40 ligand : CD40 interactions. Both Black et al. and Wilson et al. teach inhibitory anti-CD40 ligand (anti-gp39) antibodies and their effects on T cell mediated activation and functions. Given the role of various cytokines such as IL-2, IL-4 and γ-interferon, which were known to be products of the T cells targeted by antagonistic anti-gp39 antibodies, play in immune responses, one of ordinary skill in the art would have been motivated to screen and test for the properties of antagonistic anti-CD40 ligand antibodies that inhibited T cell activation and proliferation in the selection of such inhibitory antibodies that can regulate the various manifestations of T cell activation and function.

The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983). See MPEP 2144

Applicant's arguments are not persuasive.

11. No claim allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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